EPA High Production Volume Program

(Revised)

Test Plan for

IRGANOX 1330 / ETHANOX 330

1,3,5-trimethyl-2, 4,6-tris (3,5-di-t-butyl-4-hydroxybenzyl) benzene

CAS No. 1709-70-2

November 14, 2006

Submitted by:

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And

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Executive Summary

A. Introduction

An important objective of EPA's High Production Volume (HPV) chemical challenge program is the gathering and public release of basic hazard information on chemicals imported or manufactured at high volumes in the United States. Ciba Specialty Chemicals and Albemarle Corporation have agreed to participate in this program and here submit for review and public comment the available data and test plan for Irganox 1330 / Ethanox 330.

B. General Substance Information

Chemical Name: 1,3,5-trimethyl-2, 4,6-tris (3,5-di-t-butyl-4-hydroxybenzyl) benzene

Appearance: White solid

Typical Commercial Purity: 98 – 100%

Chemical abstract Service Registry Number: CAS # 1709-70-2

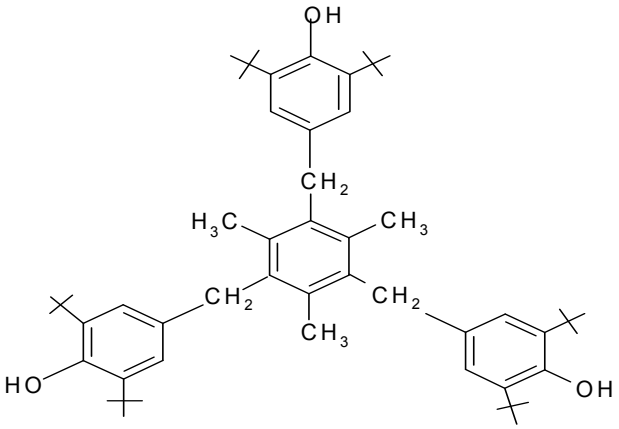
Trade Names: IRGANOX 1330 (Ciba)
ETHANOX 330 (Albemarle)

Other Synonyms / Trade Names: Ionox 330, Ethyl 330, Ethyl Antioxidant 330, AO 40

Chemical Formula: C54H78O3

Molecular weight: 775.22

Structure:



C. General Use Information

1,3,5-trimethyl-2,4,6-tris(3,5-di-t-butyl-4-hydroxybenzyl)benzene, commercially known as Irganox 1330 and Ethanox 330, is a sterically hindered phenolic antioxidant that protects organic substrates against thermo-oxidative degradation.

Irganox 1330 / Ethanox 330 is used in polyolefins (e.g., polyethylene, polypropylene, polybutene) for the stabilization of pipes, molded articles, wires and cables, dielectric films and in other polymers such as engineering plastics like linear polyesters, polyamides, and styrene homo- and copolymers. It may also be used in PVC, polyurethanes, elastomers, adhesives, and other organic substrates.

This product has been regulated by the FDA for use in all polymers at a maximum level of 0.5% except for nylon resins where the maximum use level is 1%. The resultant polymers would conceivably contact all food types with no temperature restrictions.

Sales of Irganox 1330 / Ethanox 330 are to industrial users only. The polymer industry has a record of safe use of additives such as Irganox 1330 / Ethanox 330 and worker exposures are considered minimal. Industrial Hygiene programs and Responsible Care® practices are the norm throughout the industry and it is the experience of Ciba Specialty Chemicals and Albemarle Corporation that customers handle such products in a careful and conscientious manner. Material Safety Data Sheets (MSDS) are distributed that present detailed hazard data and provide directions for safe handling. After Irganox 1330 / Ethanox 330 is incorporated in the polymer matrix it is relatively immobile and release-exposure to humans or the environment is considered minimal.

Environmental Endpoints:

Ecotoxicology testing for Irganox 1330 / Ethanox 330 indicates the compound has low toxicity to fish, aquatic plants and aquatic invertebrates. Aquatic toxicity testing was conducted with water loadings well above the solubility limits of the compound; these test conditions provide a worst-case challenge to the test organisms and indicate that there is low concern for environmental effects. Furthermore, under environmental conditions the low solubility of the material (< 1mg/L) should preclude the occurrence of acutely toxic exposures. The compound has a calculated n-octanol-water coefficient (log Pow) of > 6. Based on this and its other physical-chemical properties, the substance in the environment is likely to bind to the soil and sediment where it is expected to be immobile and have limited bioavailability. The material is not readily biodegradable. Based on its present commercial use, environmental release and exposures are expected to be negligible.

Toxicology Endpoints:

Available mammalian acute toxicity data indicates the compound has very low toxicity by oral, dermal, or inhalation exposure. In a 90-day toxicity study in the rat with dietary concentrations up to 31,600 ppm, there were no significant adverse effects up to 10,000 ppm. In 15-week toxicity studies with rats and dogs, there were no significant effects observed and a dietary NOEL greater than 5000 ppm was indicated. In 2-year carcinogenicity studies, neither tumors nor lesions were observed with dietary exposures ranging from 400 to 10,000 ppm. Repeat dose testing consistently shows that Irganox 1330 / Ethanox 330 does not have adverse effects on reproductive organs, even at relatively high exposure levels, and multi-generation reproduction testing did not demonstrate significant toxicity or teratogenic potential. Genetic toxicity testing has shown that the compound is not mutagenic. A chromosomal aberration study is not available, however, Irganox 1330 / Ethanox 330 has been evaluated in long-term carcinogenicity testing in rats and mice which does not show a tumorigenic response or other significant adverse health effects. These data support a very low concern for clastogenic effects and indicate that a chromosome aberration study is not needed to access the risk of this compound.[1]

Conclusions

The available data are sufficient to meet the requirements of the HPV challenge program.

[1] Irganox 1330 / Ethanox 330 is structurally related to several hindered phenol antioxidants also involved in the HPV program which have not shown clastogenic effects (notably CAS 6683-19-8, CAS 27676-62-6 and CAS 2082-79-3). For additional supporting data relating to hindered phenol antioxidants, also see information presented for the HPV Hindered Phenol Category, sponsored by the American Chemistry Council, should also be reviewed.

SUMMARY TABLE

CAS NO. 1709-70-2	DATE	RESULTS	FULFILLS REQUIREMENT
PHYSICAL/CHEMICAL ELEMENTS			
Melting Point	1972	246 ^{o}C	Yes
Boiling Point	2004	821.96 °C	Yes
Vapor Pressure	2004	3.14 x 10 $^{-22}$ mm Hg (estimated) 1.3 x 10^{-12} Pa (measured)	Yes
Partition Coefficient	2004 1988	log Kow > 17.17 (estimated) log Kow > 6.0 (measured)	Yes
Water Solubility	1992 2003	< 1 mg / liter (measured) 9.11 x 10^{-14} mg/ L (estimated)	Yes
ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS			
Photodegradation	2004	For reaction with hydroxyl radical, predicted rate constant = 150.13 x 10^{-12} cm^3/molecule-sec. Predicted half-life = 0.855 hours	Yes
Stability in Water	2006	EPIWIN model could not evaluate this structure. Experimental determination is not practical due to low water solubility.	Technical discussion
Fugacity	2004	Predicted distribution using Level III fugacity model Air 0.0134 % Water 1.26 % Soil 32.8 % Sediment 66 %	Yes
Biodegradation	1988	Not biodegradable 10 mg/L: 6% in 28 days 20 mg/L: 16% in 28 days	Yes
ECOTOXICITY ELEMENTS			
Acute Toxicity to Fish	1988	Zebra Fish : LC_{50} (96 h) > 100 mg/L	Yes
Toxicity to Aquatic Plants	1988	EC_{50} (0-72 h) > 100 mg/L	Yes
Acute Toxicity to Aquatic Invertebrates	1988	EC_{50} (24 h) > 100 mg/L	Yes

SUMMARY TABLE (CONTINUED)

CAS No. 1709-70-2	DATE	RESULTS	FULFILLS REQUIREMENT
HEALTH ELEMENTS			
Acute Toxicity	1965	Rat: LD_{50} (Oral) > 5,000 mg/kg	Yes
	1992	Rabbit: LD_{50} (Dermal) > 2,000 mg/kg	
	1983	Rat: LD_{50} (Inhalation) > 1,000 mg/ m^3	
Genetic Toxicity • Gene Mutation	1984	Ames Test - Salmonella typhimurium: No increase in mutations with or without metabolic activation (at doses of 0, 0.05, 0.1, 0.2, 0.5, 1.0, and 2.0 mg/ plate)	Yes
• Chromosome Aberration		Carcinogenicity/chronic testing is available as well as data exist for structurally similar compounds	No requirement
Repeat Dose Toxicity: i) 15 Week oral toxicity study in rats	1966	NOEL > 5000 ppm	Yes
ii) 15 Week oral toxicity study in dogs	1966	NOEL >5000 ppm	
iii) 90-day oral toxicity study in rats	1965	NOAEL = 10,000 ppm	
Chronic Toxicity/Carcinogenicity: i) 2-Year Oral Toxicity Study in Rats and Mice	1969	NOEL = 5000 ppm No tumors, lesions were observed	Yes
ii) 2-Year Oral Toxicity Study in Dogs	1968	NOEL = 10,000 ppm No tumors, lesions were observed	
iii) 2-Year oral toxicity study in rats	1968	NOEL = 2000 ppm NOAEL = 10000 ppm	
Reproductive and Developmental Toxicity	1970	No significant effects on reproduction or development in a three-generation study. NOEL = 5000 ppm	Yes